Case 2: Monoarthritis in a four-year-old child

A four-year-old Canadian-born child presented with left knee pain and swelling of two months' duration. He had experienced up to 2 h of pain and early morning stiffness. Similar symptoms had occurred four months previously, which resolved after 48 h. There was no history of trauma, rash, mouth ulcers, fever, cough, weight loss, night sweats, or pain or stiffness in other joints. He was otherwise healthy with no significant past medical history.

The musculoskeletal examination revealed a large effusion, warmth and tenderness of the left knee. There was an approximately 15° flexion contracture, and flexion was reduced to approximately 110°. The remainder of the physical examination was normal.

Radiographs of the knee showed growth disturbance suggestive of hyperemia, epiphyseal overgrowth and a small effusion. The white blood cell count was 12.3×10^9/L (normal 5×10^9/L to 12×10^9/L), hemoglobin level 130 g/L (normal 110 g/L to 140 g/L), platelet level 319×10^9/L (normal 150×10^9/L to 400×10^9/L) and his erythrocyte sedimentation rate was 3 mm/h.

The antinuclear antibody and rheumatoid factor tests were negative. An ophthalmological evaluation did not reveal uveitis. A presumptive diagnosis of oligoarticular juvenile idiopathic arthritis was made. There was minimal response to naproxen and only transient mild improvement with an intra-articular injection of corticosteroids. Synovial fluid analysis revealed a leukocyte count of 9.88×10^9/L with neutrophilic predominance (73% neutrophils, 23% lymphocytes and 4% monocytes). Five months after the onset of symptoms, and 10 weeks after initial presentation, two additional tests were performed that established the diagnosis.

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CASE 2 DIAGNOSIS: TURBERCULOUS ARTHRITIS

On further review of the patient's history, it was established that the parents had immigrated from India and that the child, while born in Canada, lived in India from four to 16 months of age. He had not received the Bacille Calmette-Guérin vaccine. There was no known contact with tuberculosis (TB) in Canada or India.

A tuberculin skin test (TST) produced 15 mm of induration at 48 h. Based on this finding, a synovial biopsy was immediately requested and performed within one week. Repeat synovial fluid analysis showed 3.630×10^9/L leukocytes (6% neutrophils, 88% lymphocytes, 4% monocytes and 2% macrophages). The synovial biopsy was analyzed for mycobacteria through histology, acid-fast bacilli staining and mycobacterial culture. Histology of the synovial biopsy demonstrated granulomatous synovitis. No mycobacteria were seen on acid-fast bacilli stain, but culture of the synovium was positive for drug-sensitive *Mycobacterium tuberculosis*. A chest radiograph was normal and a magnetic resonance imaging scan of the left knee demonstrated marked thickening and enhancement of the synovium, with a moderate joint effusion and enlarged lymph nodes in the popliteal fossa.

Detailed contact investigation identified an elderly close contact with smear-negative, culture-positive, pulmonary TB. Her *M tuberculosis* strain was molecularly identical to our patient's by spoligotyping.

Following diagnosis, treatment with isoniazid, rifampin, pyrazinamide, ethambutol and vitamin B_6 was initiated. Once the strain was confirmed to be fully susceptible, ethambutol was discontinued. The patient was also treated with naproxen and physiotherapy with nighttime splinting but had ongoing contracture and functional limitation. For this reason, a second intra-articular steroid injection was performed after 10 weeks of anti-TB therapy, which led to significant reduction in pain and increased mobility.

Peripheral joint involvement with *M tuberculosis* is rare. There were nine million new TB infections in 2010 (WHO data), and of those, an estimated 2% had osteoarticular involvement, most commonly involving the spine (1). Tuberculous arthritis of the knee is typically caused, as in our patient, by hematogenous seeding of the joint. An aseptic reactive arthritis from an extra-articular source of TB, termed Poncet's disease, has been described. Direct TB infection of the knee has been reported in fewer than 100 children (1) but is likely underreported.

The heterogeneous clinical presentation and rarity of tuberculous arthritis contribute to its diagnostic difficulty. The typical presentation is a subacute or chronic monoarthritis. Synovial fluid analysis is nonspecific, in which the cell predominance, as in our case initially, may be neutrophilic or lymphocytic. Chest radiographs are often normal, but the presence of hilar adenopathy or parenchymal disease should raise ones clinical suspicion. The TST will almost universally become positive but may be negative initially (1). In addition, interpretation of the TST remains difficult in those who have received the Bacille Calmette-Guérin vaccine.

Clinical suspicion is critical in helping to establish the diagnosis. Risk factors include known contact with TB, and the child or parents originating from an Aboriginal community, a TB-endemic country or visits to such countries. While the TST and history may suggest the diagnosis, a synovial biopsy is essential both for histology and to culture the organism for drug sensitivities to guide therapy. Early diagnosis is important to prevent long-term disability from joint destruction.

The optimal duration of therapy has not been established. A literature review of treatment for osteoarticular TB revealed relapse rates of 2.1% to 4.3%, and 0.74% with six to 11 months and ≥12 months of therapy, respectively (2). Referral to or consultation with a TB specialist is recommended to assist with treatment decisions. Once effective anti-TB therapy is established, some authors suggest a role for intra-articular corticosteroids as an adjunct in tuberculous arthritis. While there are no human data beyond case reports, some animal studies suggest a chondroprotective effect (1).

CLINICAL PEARLS

- The presentation of *Mycobacterium tuberculosis* arthritis can mimic that of monoarticular juvenile idiopathic arthritis.
- Synovial fluid analysis and culture, as well as imaging, are often nondiagnostic and synovial biopsy for mycobacterial culture is necessary to establish a diagnosis of tuberculous arthritis.
- TB in a child is often a sentinel event and should prompt detailed contact tracing to identify an infectious source case.

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